ASTRO-LAB

AN FP7-SUPPORTED PROJECT TO INVESTIGATE THE SAFETY OF THERAPY IN ASTHMA, WITH A FOCUS ON ADHERENCE

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"ASSESSMENT OF THE SAFETY OF LABAs (Long Acting Bronchodilators) IN ASTHMA IN ROUTINE CARE BY COMBINING HEALTH-CARE DATABASES AND DIRECT PATIENT FOLLOW-UP: ASTRO-LAB"

Participants

Part. No.	Scientific responsability	Participant legal name	Country	Organisation type
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2	Richard HUBBARD	Nottingham University (UON)	UK	University
3	Stephane SCHÜCK	KAPPA Santé (KS)	FR	SME
4	Hassy DATTANI	Epic Database Research Company Ltd (CSD MR UK)	UK	Private Company
5	Marijn DE BRUIN	Wageningen University (WU)	NL	University
6	Montserrat FERRER FORES	Consorci Mar Parc de Salut (PSMAR)	ES	Public research centre
7	Javier OLAIZ	Lyon Ingénierie Projets (LIP)	FR	SME

Calender: 2012-2015

WP	tasks	Year 1											Year 2												Year3												Year 4											
		M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18	M19	M20	M21	M22	M23	M24	M25	M26	M27	M28	M29	M30	M31	M32	M33	M34	M35	M36	M37	M38	M39	M40	M41	M42	M43	M44	M45	M46	M47	M48
WP1	Project Managment																																																
	Preparing contractual documents, procédures																																																
	Kick off / mid term / final meetings																																																
	Project website construction																																																
	Periodic managment report																																																
	Periodic activity report																																																
	Managment support/ administrative coordination																																																
WP2	Conception																																																
	Literature synthesis																																																
	Protocol and CRF writing																																																
	Advisory board 1 : protocole and CRF validation																																																
	CRF testing and protocol and CRF finalisation																																																
	Ethics /regulatory authorisations in France / UK																																																
	Internet Website development																																																
	Study material conception																																																
	Monitoring Data Base development																																																
	CATI procedures writing and testing																																																
WP3	Drug exposure validation and adherence measurement																																																
	Adherence literature synthesis																																																
	Choice of scales																																																
	Adherence determinant tools																																																
	Linkage prescription /delivery data authorisation																																																
	Linkage prescription and delivery data																																																
	Algorithm for adherence and drug exposure																																																
	Advisory board 2: Algorithm discussion																																																
	Algorithm report																																																
WP4	Prospective Cohort Management																																																
	Sampling from the prescription database																																																
	Study material																																																
	Contact GPs for agreement to participate																																																
	Contact patients for agreement to participate																																																
	GPs and patients set up for the study																																																
	GPs questionnaire at inclusion																																																
	Monitoring																																																
	CATI quaterly interview																																																
	Questionnaires completion on Internet website																																																
	Data Management																																																
	Database lock																																																
WP5	Safety and Impact Analysis																																																
	Stsatistical analysis plan (SAP)																																																
	Advisory board 3 (Stastistical plan validation)																																																
	Safety analysis																																																
	Adherence analysis																																																
	Population impact modelisation																																																
	Advisory board 4 (analysis presentation)																																																
	Final report																																																
WP6	quaterly newsletter																																																
	abstract/ publication / attendance to congress																																																
	symposium																																																

Political context (1/3)

1. PEL: expertise in asthma therapy
2. PEL: expertise in Pharmacoepidemiology (fenoterol & McGill, PHARMO)
3. 2008: EnCEPP at EMA
4. June 2010 : collaboration EMA & DG Research for the 5th call FP7
5. July 2010 : EMA organises a meeting in the context of the 5th call, emphasising the need for and the role of SMEs
6. August 2010: informal contacts with EMA/EnCEPP: any chance?

Political context (2/3)

7. Sept –Oct 2010: writing of a project by David (épidemiologist, KS), Marijn (adherence, WU), and Eric, with support < LIP & Kappa Santé

8. November 2010: submission of the ASTRO-LAB project

9. December 2010: networking (EMA)

10. Feb 2011: project « might be » accepted

11. May 2012: nego with Brussels (DOW)

'Political context' (3/3)

12. June 2012: « final approval » to start in December 2012

13. Some « problems »:
    - Money : late arrival (Jan)… consequences…
    - Contract : idem… consequences…
    - Kappa Sante : distinct roads < Fall (EGB)
    - Partners: 'illness' of a boss

14. KOM in Feb 2012

15. Start of activities in March, and discovery of « reality »….

Therapeutic context (1/2)

- Asthma = inflammatory disorder (acute exacerbations of chronic inflammation)

- Exacerbations « favoured » by irregular/low exposure to « the » anti-inflammatory therapy, inhaled steroids (ICS)

- ICS often 'poorly' used < patients (corticophobia, lack of immediate effects, lack of training, ...), which may lead to SAEs (oral steroids, hospital contacts, deaths)

- Other controllers devoid of AI actions, LABAs, are much appreciated as a result of their bronchodilatory effects (QOL)

Therapeutic Context (2/2)

- Studies & M-A looking at the safety profile of LABAs have resulted in contradictory findings, particularly when LABAs are used together with ICS, in « FDC », or as two distinct canisters

- However, « signals » suggest a potential risk of SAEs with LABAs, with the methodological issue that such SAEs are similar after 'under-exposure to ICS' after an acute exacerbation induced by an external 'trigger' (typically : infection)

- EU and US Regulators have identified the safety of LABAs as a priority in PH research

Main Objective

To compare in real-life settings the rates of SAEs in kids and in adults treated with LABAs (alone, or in association to ICS) to the rates observed in persons treated with ICS alone, after adjusting for severity

Main Deliverable=
Cohort of Asthma Patients

i. To conduct a prospective cohort study linking general practice databases, national claims databases, and primary data collection with a study design which addresses the methodological gaps identified in the literature review.

Tested Hypothesis

Is the use of LABAs by asthma patients (cave COPD!) associated, in real life settings, to the occurrence of SAEs (oral steroids, hospital contacts, deaths)?

Adherence to ICS= confounder

- LABAs are in most instances (>95%) used with ICS, the only therapy able to prevent exacerbations

- But, irregular use of ICS may lead to SAEs

- **In the analyses of SAEs, we must distinguish what might be due to LABAs (tox?), from what might be due to irregular use of ICS**

- Indeed, adherence to ICS = major confounder

Use of LABAS and ICS

Four groups will be identified

- Patients with LABAs only
- Patients with ICS only
- Patients with LABAs and ICS (distinct canisters)
- Patients with LABAs and ICS (1 canister, FDC)
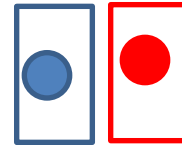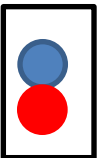
Methods & population

- Cohort study, with 24 months FU

- Patients (6-40 yrs) will be preselected in France (bases CNGE*) and in the UK (THIN) from their asthma therapy

- 1 500 kids (6-13 yrs) & 1 500 adults (14-40 yrs) will be selected

* Collège National des Généralistes enseignants

Data Collection

- Prospective collection using 3 sources:

  - Prescribing data (CNGE in France, THIN in the UK, EMRs)

  - Claims data (SNIIRAM in France)

  - Patients Reported Outcomes (adherence, SAEs) in the 2 countries, using CATIs

- Linkage will be performed by a TTP

Analyses planned

Three complementary approaches:

1- Preliminary analyses according to 'initial' group (« ITT »)

2- Analyses with time-dependent variables (cf switches)

3- Case-cross over study

MESSAGES

- ## Before the Application
  - Identify the right **persons** (science)
  - Identify the right « **mix** » (public/private)
  - Identify the right « **writers** » of the project
  - Identify the right « **reasoning** »: innovative, 'risk-taking' (reasonable!), improving our knowledge basis, tackling the 'key remaining issue' (look at adherence, idiot!)
  - **Verify** acceptability/political and scientific correctness/
  - **Nertwork!** (the project & you must be known!)

MESSAGES

- After the Application
  - Expect the unexpected!
  - Do not take risks! (some bureaucracy)
  - Prioritise! (first CA, other admin documents)
  - Disentangle the big project in a large N of small projects (minimal size)
  - Play the orchestra leader (or the « Maitresse », with her kids)
  - In one word, « Alice »